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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,865	11/20/2003	Nobuya Matsuoka	245748US0CONT	5646

22850 7590 02/10/2006

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EXAMINER	
LEWIS, AMY A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,865	MATSUOKA ET AL.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. PCT/JP00/03015.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *A-B*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *1/23/06* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Case

The Preliminary Amendment, filed 20 November 2003, has been entered into the application. Accordingly, claims 1-18 have been amended, claims 19-38 have been added, and the specification has been amended to change the title and include related application information. In addition, the status letters, filed 29 April 2004 and 10 November 2005, have been acknowledged. The examiner for the instant family of applications has changed; the current examiner assigned to this application is Amy A. Lewis.

Claims 19-38, as filed 20 November 2003, are presented for examination.

Claim 31 will be examined according the chemical structure provided in the facsimile provided by Thomas Cunningham on 23 January 2006 at the request of the Examiner (see also the interview summary).

Priority

Acknowledgement is made of Applicant's claim for foreign priority, under 35 U.S.C. § 119(a)-(d), to Japanese Application No. 11/131108, filed on 12 May 2000; the certified copy was filed in PCT Application No. PCT/JP00/03015 application on 11 May 2000.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 19-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Akahane et al. (WO 98/03507).

Akahane teaches a pharmaceutical composition for the treatment of Parkinson's disease comprising a compound of formula (I) (see: abstract; claims 1-9, 11, 13, and 14). The reference teaches the instantly claimed compound of the formula in claims 32-34 (see: abstract, claims 1-9). In addition, Akahane teaches a compound which meets the requirements of the compound of instant claim 31 (see pages 9-10 regarding compound If). The reference teaches that the pyrazolopyridine compounds of formula (I) are adenosine antagonists (abstract, claim 14). Regarding the limitations of the compound as an A_1A_{2a}-receptor dual antagonist and various IC_{50} values (see instant claims 23-26), these activities are an inherent property of the compound and confer no patentable weight.

It is established that compounds inherently possessing a utility anticipate claims directed to that utility (see *Ex parte Novitski 26 USPQ2nd 1389*). Akahane teaches the same compounds as instantly claimed for use in the treatment of Parkinson's disease; such treatment would reasonably encompass the treatment of symptoms of the disease.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2) Claims 19-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating catalepsy (in mice), ameliorating impaired-memory (in male SD rats), and anxiety-like behavior (in Wistar rats), with the compound 3-[2-(thiazol-2-ylmethyl)-3-oxo-2,3-dihydro-pyridizin-6-yl]-2-phenylpyrazolo [1,5-a]pyridine (hereinafter referred to as the compound of claim 31), does not reasonably provide enablement for treating Parkinson's disease and the prevention and/or treatment of the concomitant symptoms thereof with all A_1A_{2a}-receptor dual antagonists, including those represented by the instantly claimed generic formula (see for example claim 29). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) Nature of the invention.
2) State of the prior art.
3) Relative skill of those in the art.
4) Level of predictability in the art.

5) Amount of direction or guidance provided by the inventor.
6) Presence or absence of working examples.
7) Breadth of the claims.
8) Quantity of experimentation necessary to make or use the invention based on the content of the disclosure.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1) The nature of the invention.

The claimed invention relates generally to treatment of Parkinson's disease, and specifically to compositions and methods for treating concomitant symptoms thereof.

2) State of the prior art & 4) Level of predictability in the art.

While the state of the art is relatively high with regard to reducing the severity of symptoms of Parkinson's disease, such as treating dyskinesias with the drug levodopa in the early stages of the disease, the state of the art with regard to treating the underlying cause of Parkinson's disease (i.e. neurodegeneration due to loss of dopamine neurons) broadly is underdeveloped (See Wu SS and Frucht SJ, "Treatment of Parkinson's Disease: What's on the horizon?," 2005 *CNS Drugs* 19(9): 723-743).

Further, current treatments are "hampered by long-term motor complications [and] on-off fluctuations, wearing-off and disabling dyskenisias limit the smooth benefit seen initially" (Wu and Frucht, p. 725). Thus, treating of symptoms of Parkinson's disease involves a very high level of unpredictability. The lack of significant guidance from the present specification or prior art with regard to the actual treatment of all types of cancer cells in a mammal, including a human subject, with the claimed active

ingredients makes practicing the claimed invention unpredictable.

In addition, the state of the art is also relatively high regarding experiment models of Parkinson's disease and Parkinson's pathologies, each having various strengths and weaknesses depending on the question being investigated (for example loss of dopamine neurons versus severity and type of symptoms). (See: Bové J, et al., "Toxin-induced models of Parkinson's Disease," July 2005 *NeuroRx* 2: 484-494).

3) Relative skill of those in the art.

The relative skill of those in the art is high, generally that of a PHD/MD.

5) Amount of direction or guidance provided by the inventor & 6) Presence or absence of working examples.

The specification at pages 66-68, Tests 1-3 specifically teach 1) the treatment of catalepsy (in mice), 2) reduction of anxiety-like behavior in terms of the total duration of social interaction time (in Wistar rats), and 3) ameliorating impaired-memory (in male SD rats), with the compound of claim 31.

7) Breadth of claims.

The claims are very broad and inclusive of treating Parkinson's disease and treating and/or preventing the *all* concomitant symptoms thereof in general. The breadth of the claims exacerbates the complex nature of the subject matter to which the present claims are directed. The claims are extremely broad due to the vast number of possible symptoms which may be associated with the disease.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification does not enable any person skilled in the art to which it pertains (i.e. treatment of Parkinson's disease and it's concomitant symptoms) to make or use the invention commensurate in scope with the claims. The lack of adequate guidance from the specification or prior art with regard to the actual treatment of all symptoms with A_1A_{2a}-receptor dual antagonists, including those represented by the instantly claimed generic formula, fails to rebut the presumption of unpredictability existent in this art. Applicants fail to provide the guidance and information (such as dosage and schedule) required to ascertain which A_1A_{2a}-receptor dual antagonists will treat which symptoms without resorting to undue experimentation. Applicant's limited disclosure with respect catalepsy, reduction of anxiety-like behavior in terms of the total duration of social interaction time, and ameliorating impaired-memory (see the specification at pages 66-68, Tests 1-3) is noted but does not demonstrate treating Parkinson's disease and any or all of it's concomitant symptoms.

Prevention:

Regarding claim 37, the burden of enabling the prevention of a condition such as Parkinson's disease would be much greater than that of enabling the treatment of concomitant symptoms of the condition. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of preventing Parkinson's disease or how a patient could be kept from every being susceptible to this condition. Nor is there any guidance provided as to a specific protocol

to be utilized in order to show the efficacy of the presently claimed active agents for preventing Parkinson's disease.

The term "prevention" is synonymous with the term "curing" and both circumscribe methods of absolute success. Since absolute success is not reasonably possible with most diseases/conditions, especially those having etiologies and pathophysiological manifestations as complex as Parkinson's disease, the specification, which lacks an objective showing that Parkinson's disease can actually be prevented, is viewed as lacking an adequate written description of the same.

It is noted that there was discussion regarding recitation of "prevention" of Parkinson's disease versus prevention of concomitant symptoms thereof during prosecution of Application Serial No. 09/926469, and that the 35 USC 112 first paragraph rejection was withdrawn. However, in the instant application, claim 37 encompasses prevention of Parkinson's disease as well as concomitant symptoms thereof. It should also be noted that claim 31 is drawn to a pharmaceutical composition; therefore the intended use of the composition confers no patentable weight.

Absent a reasonable *a priori* expectation of success for using a specific chemotherapeutic agent/combination to treat any particular type of cancer, one skilled in the art would have to extensively test many various tumor types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice

the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Pertinent Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

- US Patent Application Publication US 2004/0152706 A1 (Akahane A and Tanaka A), teaches the instantly claimed compounds as adenosine antagonists for treatment of Parkinson's disease. See abstract and claims.

- Vu CB, et al., "Piperizanie derivatives of [1,2,4]triazolol[1,5-a][1,3,5]triazine as potent and selective adenosine A2a receptor antagonists," 2004 *J Med Chem* 47: 4291-4299. The reference teaches various piperazine derivatives similar to the instantly claimed compounds as adenosine A2a antagonists. In particular, several compounds were effective in rodent models of Parkinson's disease. And one compound was active in the rodent catalepsy model.

Conclusion

Claims 19-38 are rejected. No claims are allowed.

Contact Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is (571) 272-2765. The examiner can normally be reached on Monday-Friday, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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